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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,641	03/01/2002	Paul Barth Conrad	STRATA-06663	3731

7590 07/29/2003

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EXAMINER

DAVIS, RUTH A

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/087,641

Applicant(s)

CONRAD ET AL.

Examiner

Ruth A. Davis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 05 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1 – 14 in Paper No. 8 is acknowledged.

Claims 15 – 63 have been cancelled. Claims 1 – 14 are pending and have been considered on the merits.

Claim Objections

2. Claims 3 and 6 are objected to because of the following informalities: In claim 3, the term "NIKS" should first be spelled out followed by the abbreviation in parentheses. In claim 6, the term "NHDF" should first be spelled out followed by the abbreviation in parenthesis. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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In claim 3, the term "NIKS" should first be spelled out followed by the abbreviation in parenthesis.

In claim 6, the term "NHDF" should first be spelled out followed by the abbreviation in parenthesis.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 – 4, 6 and 12 – 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Allen-Hoffmann et al. (US 5989837).

Applicant claims a method for preparing a seeded dermal equivalent, the method comprising providing a dermal equivalent, keratinocytes and culture media having an air interface; culturing the dermal equivalent in the media; lifting the dermal equivalent to the air interface; and seeding the dermal equivalent with the keratinocytes to provided a seeded dermal equivalent. The keratinocytes are selected from primary human keratinocytes, and immortalized keratinocytes, specifically wherein the immortalized keratinocytes are NIKS. The dermal equivalent comprises collagen and fibroblasts and the fibroblasts are NHDF cells. The method further comprises incubating the seeded dermal equivalent such that a skin equivalent is formed, wherein the skin equivalent is stratified into squamous epithelia.

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Allen-Hoffmann teaches a method for making a stratified squamous epithelia (abstract) wherein NIKS (see abstract, col.3 line 45-52) cells (immortalized keratinocytes) are seeded onto a base dermal equivalent of collagen and normal human fibroblasts (col.4, line 57-60). The dermal equivalent is lifted to the air interface to provide a lifted dermal equivalent (col.15, line 20-39).

The method anticipates the claimed subject matter.

7. Claims 1 – 2, 4 – 9 and 12 – 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang et al. (2000).

Applicant claims a method for preparing a seeded dermal equivalent, the method comprising providing a dermal equivalent, keratinocytes and culture media having an air interface; culturing the dermal equivalent in the media; lifting the dermal equivalent to the air interface; and seeding the dermal equivalent with the keratinocytes to provided a seeded dermal equivalent. The keratinocytes are selected from primary human keratinocytes and immortalized keratinocytes, and the dermal equivalent comprises collagen and fibroblasts. Specifically the collagen is rat tail tendon collagen and the fibroblasts are NHDF cells. The lifting step further comprises incubating the lifted dermal equivalent to the air interface for at least 6, 12 or 18 hours before seeding. The method further comprises incubating the seeded dermal equivalent such that a skin equivalent is formed, wherein the skin equivalent is stratified.

Yang teaches a method for making a stratified skin equivalent, wherein the method comprises layering a dermal matrix of fibroblasts and collagen with keratinocytes and culturing the dermal equivalent at the air-liquid interface (abstract). Specifically, rat tail tendon collagen

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was combined with normal human fibroblasts to create the dermal equivalent which was seeded with keratinocytes (p.8, collagen and cells). The dermal equivalent was lifted prior to seeding (p.9, preparation of dermal equivalent). The skin was made by seeding keratinocytes onto the dermis, and was further cultured at the air-liquid interface (p.10, production of artificial skin).

The reference anticipated the claimed subject matter.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1 – 2 and 4 – 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang.

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Applicant claims a method for preparing a seeded dermal equivalent, the method comprising providing a dermal equivalent, keratinocytes and culture media having an air interface; culturing the dermal equivalent in the media; lifting the dermal equivalent to the air interface; and seeding the dermal equivalent with the keratinocytes to provided a seeded dermal equivalent. The keratinocytes are selected from primary human keratinocytes and immortalized keratinocytes, and the dermal equivalent comprises collagen and fibroblasts. Specifically the collagen is rat tail tendon collagen and the fibroblasts are NHDF cells. The lifting step further comprises incubating the lifted dermal equivalent to the air interface for at least 6, 12 or 18 hours before seeding, or for about 24 or 6 – 24 hours. The method further comprises incubating the seeded dermal equivalent such that a skin equivalent is formed, wherein the skin equivalent is stratified.

Yang teaches a method for making a stratified skin equivalent, wherein the method comprises layering a dermal matrix of fibroblasts and collagen with keratinocytes and culturing the dermal equivalent at the air-liquid interface (abstract). Specifically, rat tail tendon collagen was combined with normal human fibroblasts to create the dermal equivalent which was seeded with keratinocytes (p.8, collagen and cells). The dermal equivalent was lifted prior to seeding (p.9, preparation of dermal equivalent). The skin was made by seeding keratinocytes onto the dermis, and was further cultured at the air-liquid interface (p.10, production of artificial skin).

Yang does not teach the method wherein the incubating lasts for about 24 hours, or 6 – 24 hours. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize incubation times as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art

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would have been motivated by routine practice to optimize the incubation times of Yang with a reasonable expectation for successfully making a stratified skin equivalent.

11. Claims 1 – 4 and 6 – 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allen-Hoffmann.

Applicant claims a method for preparing a seeded dermal equivalent, the method comprising providing a dermal equivalent, keratinocytes and culture media having an air interface; culturing the dermal equivalent in the media; lifting the dermal equivalent to the air interface; and seeding the dermal equivalent with the keratinocytes to provided a seeded dermal equivalent. The keratinocytes are selected from primary human keratinocytes, and immortalized keratinocytes, specifically wherein the immortalized keratinocytes are NIKS. The dermal equivalent comprises collagen and fibroblasts and the fibroblasts are NHDF cells. The method further comprises incubating the seeded dermal equivalent such that a skin equivalent is formed, wherein the skin equivalent is stratified into squamous epithelia. The lifting step further comprises incubating the lifted dermal equivalent to the air interface for at least about 6, 12 or 18 hours before seeding, or about 24 or 6 – 24 hours.

Allen-Hoffmann teaches a method for making a stratified squamous epithelia (abstract) wherein NIKS (see abstract, col.3 line 45-52) cells (immortalized keratinocytes) are seeded onto a base dermal equivalent of collagen and normal human fibroblasts (col.4, line 57-60). The dermal equivalent is lifted to the air interface to provide a lifted dermal equivalent (col.15, line 20-39).

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Allen-Hoffman does not teach the methods with the claimed incubation times. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize incubation times as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the incubation times of Allen-Hoffmann with a reasonable expectation for successfully making a stratified skin equivalent.

12. Claims 1 – 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Allen-Hoffman.

Applicant claims a method for preparing a seeded dermal equivalent, the method comprising providing a dermal equivalent, keratinocytes and culture media having an air interface; culturing the dermal equivalent in the media; lifting the dermal equivalent to the air interface; and seeding the dermal equivalent with the keratinocytes to provided a seeded dermal equivalent. The keratinocytes are selected from primary human keratinocytes, and immortalized keratinocytes, wherein the immortalized keratinocytes are NIKS. The dermal equivalent comprises collagen and fibroblasts, specifically rat tail tendon collagen and NHDF cells. The lifting step further comprises incubating the lifted dermal equivalent to the air interface for at least about 6, 12 or 18 hours before seeding; or alternatively 24 or 6 – 24 hours. The method further comprises incubating the seeded dermal equivalent such that a skin equivalent is formed, wherein the skin equivalent is stratified into squamous epithelia.

Yang teaches a method for making a stratified skin equivalent, wherein the method comprises layering a dermal matrix of fibroblasts and collagen with keratinocytes and culturing

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the dermal equivalent at the air-liquid interface (abstract). Specifically, rat tail tendon collagen was combined with normal human fibroblasts to create the dermal equivalent which was seeded with keratinocytes (p.8, collagen and cells). The dermal equivalent was lifted prior to seeding (p.9, preparation of dermal equivalent). The skin was made by seeding keratinocytes onto the dermis, and was further cultured at the air-liquid interface (p.10, production of artificial skin).

Yang does not teach the method wherein NIKS cells are used or wherein the stratified skin is squamous epithelia. However, Allen-Hoffmann teaches a method for making a stratified, squamous epithelia (abstract) wherein NIKS (see abstract, col.3 line 45-52) cells (immortalized keratinocytes) are seeded onto a base dermal equivalent of collagen and normal human fibroblasts (col.4, line 57-60). The dermal equivalent is lifted to the air interface to provide a lifted dermal equivalent (col.15, line 20-39). At the time of the claimed invention, one of ordinary skill in the art would have been motivated to use the keratinocytes of Allen-Hoffmann in the methods of Yang because Allen-Hoffmann teaches the cultures are useful in tissue engineered products (col.4 line 14-21). In addition, one of ordinary skill in the art would have been motivated to make the stratified skin of Yang into squamous epithelia because it was known to be effective for skin models, as evidenced by Yang and Allen-Hoffmann. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to use the keratinocytes of Allen-Hoffmann in the methods of Yang with a reasonable expectation for successfully making a dermal/skin equivalent.

The references do not teach the methods with the claimed incubation times. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize incubation times as a matter of routine experimentation. Moreover, at

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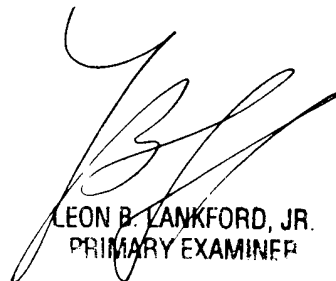
the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the incubation times of Yang and/or Allen-Hoffmann with a reasonable expectation for successfully making a stratified skin equivalent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
July 25, 2003



LEON B. LANKFORD, JR.
PRIMARY EXAMINER